UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,595	09/23/2002	Sunil Ahuja	4003.001600	2489

20792 7590 05/04/2006

MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,595	AHUJA ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-62* is/are pending in the application.

4a) Of the above claim(s) *38-48,61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group II, claims 49-60, in the reply filed on 7/19/2005 is acknowledged. The traversal is on the ground(s) that the examiner has not demonstrated that groups 1 and 2 do not relate to a single general inventive concept and that the reference of Brennan discloses nothing more than an alleged method of producing oligonucleotides that purportedly represent every possible 10-mer oligonucleotide, whereas claim 38 recites a composition of specific sets of nucleic acid segments have specific structural features set forth in the claims. The response asserts that the method claims of group 2 depend from claim 38 and the search is coextensive. The response also asserts that no unity of invention was raised in the international search report. This is not found persuasive because the claims require no specific structural features for the set of nucleic acids in claim 38. The set is only described functionally, and a large number of possible sequences could function as claimed. The examiner cited Brennan, as an array of all possible 10mers could be used to sequence and therefore determine the identity of haplotypes. Additionally, a kit of random hexamer nucleic acids, which have been available in the art well before the instant filing date, could be used to amplify nucleic acids containing the haplotypes, and therefore "detect", which haplotypes could be determined by sequencing. Contrary to the assertions made in the response, no actual structural limitations are provide for the nucleic acids, only that a nucleic acid be "capable of detecting each of the following haplotype groups". The claim is completely silent as to the actual sequence composition of the segment(s) and therefore recites no "specific" segment. Accordingly, the claims lack a special technical feature over the prior art and lack unity of

invention. As indicated by the previous office action, art relating to the claimed products, for example an array of nucleic acids, or kit of random hexamers, would not necessarily provide any information regarding the claimed methods, and therefore, searching is not coextensive. The fact that no unity of invention issue was raised in the PCT regarding the subject matter of the pending claims, is not relevant to the assessment of the lack unity of invention as noted above and in the previous office action. The requirement is still deemed proper and is therefore made FINAL.

Priority

2. The instant application claims the benefit of priority to provisional application 60,159,137. However, the claims are not awarded benefit of the '137 filing date because SEQ ID NO: 65 was not disclosed in the '137 application. (SEQ ID NOS 64-72 are not present in the provisional application.) Figure 3A of the '137 application does not provide bases for the complete sequence of SEQ ID NO: 65. Accordingly, the effective filing date of the instant claims is 10/12/2000.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892 or by applicant in the 1449 submitted 9/23/2002, they have not been considered.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

5. The sequence listing has been entered. It is noted, however, that SEQ ID NOS: 64-72 were not present in the '137 provisional application.

Claim Objections

6. Claims 49-60 are objected to for being dependent on withdrawn, non-examined claims.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 49-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in their dependency to claim 38. Claim 38 is drawn to a set of nucleic acids "capable of detecting each of the following haplotype groups". The claim contains a table, which refers to different haplogroups, and lists nucleotide positions in the CCR5 sequence as well as reciting "with the definition of the amino acid at position... of the human CCR2 sequence and the presence or absence of a 32 base pair deletion of the human CCR5 sequence". The claim, however, does not set forth any specific nucleic acids, nor does it make clear if each of the positions listed for CCR2 or CC5 are detected. Accordingly, the method

claims which depend from claim 38, are indefinite because it is unclear what the metes and bounds of the step of "identifying" encompass. It is not clear if the term is limited to determining the nucleotide or amino acid at EACH of the positions listed, or simply to the use of an unspecified set of nucleic acids which could be used for amplification and still meet the requirements of claim 38, but would not necessarily designate which nucleotide was at each position listed in claim 38. The claims are directed to methods whose only positive step is "using" a set of nucleic acid segments whose structural makeup is not clear. In reciting the step of "identifying the CCR5 haploytpe group", the claim does not make clear any positive active steps for identifying, and only refers to a non specific set of nucleic acids in a withdrawn claim. For example, when reading claim 49 in the context of claim 38, it appears that the claim should require identifying each position listed in the chart in claim 38, which should include the CCR2 polymorphism, however, claim 53 is directed to "further... identifying" the CCR2 polymorphism. Accordingly, the claim's reliance on an unspecified set of nucleic acids does not make clear what is being assessed to determine the "CCR5 haploytpe group" of a subject, or which of the variations listed in claim 38 (which are not present in the method claims or clearly define which positions are required to identify a specific haplotype group) need to be determined such that a practitioner would "identify the CCR5 haplotype group" of a subject.

The claims recite the term "haplotype group" or "haplogroup" and refer to claim 38, however claim 38 recites "haplogroup". Accordingly, the recitation of haplotype group appears to lack antecedent basis because it is not clear if the term "haplogroup" and "haplotype group" are used interchangeably, or if they refer to a different combination of positions with regard to the table in claim 38.

In claim 53, the recitation of "the human CCR2 polymorphisms" lacks sufficient antecedent basis as is it is unclear if such refers to the identity of the amino acid at position 64 being a V or an I, or if it refers to additional CCR2 polymorphisms.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 49-51, and 53-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Mummidi (Mummidi et al; Nature Medicine, vol. 4, July 1998, pages 786-793).

With regard to claim 49, Mummidi teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles, including detecting the CCR2 V/I mutation (claim 53) and the 32 base pair deletion in the CCR5 ORF (see Figure 1) using a set of nucleic acids (page 792, col. 2 "Genotype analysis" to page 793 para 1 first column). With regard to claims 50, 51, 54, and 55 Mummidi correlates haploytpes with HIV progression in different racial populations (see page 788, col 1-2; page 789; figure 3;). Mummidi teaches sequencing the CCR5 region from –731-+981 (para bridging pages 792-793). With regard to claim 56, Mummidi teaches correlating the disease retarding effect of the CCR5 32 base pair deletion mutation in Caucasians and African

Americans (page 790-col. 1-2) and teaches of a weak effect of the deletion and CCR5 29G. Accordingly, as all haplotypes other than HHF*1 appear to lack the 32 base pair deletion in CCR5 as listed in claim 38, Mummidi inherently correlates an increased risk of disease progression with regard to the haplotype listed in claim 56 and Caucasians. With regard to claim 57, Mummidi teaches of the disease retarding effect in African Americans of the 64I allele in CCR2 (page 790, col. 1; page 791, col 2, last para). Accordingly, as all haplotypes except for HHG*2, appear to lack the 64I allele as listed in the table in claim 38, Mummidi inherently correlates an increased risk of disease progression with regard to the haplotypes listed in claim 57 in African Americans.

It is noted that the claims are directed to methods whose only positive step is "using" a set of nucleic acid segments whose structural makeup is not set forth. In reciting the step of "identifying the CCR5 haploytpe group", the claim does not make clear any positive active steps for identifying. Accordingly, the claim's reliance on an unspecified set of nucleic acids does not make clear what is being assessed to determine the "CCR5 haploytpe group" of a subject, or which of the variations listed in claim 38 are determined. Accordingly, the claims have been given their broadest reasonable interpretation to encompass methods of determining alleles in the CCR5 and CCR2 genes as set forth by Mummidi.

11. Claims 49-51, and 53-57 are rejected under 35 U.S.C. 102(e) as being anticipated by Kaslow (US Patent, 6,372,435).

With regard to claim 49, Kaslow teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles, including detecting the CCR2 V/I mutation (claim 53) and the 32 base pair

deletion in the CCR5 ORF (see Figure 2, Figure 9) using a set of nucleic acids. With regard to claims 50, 51, 54-57 Kaslow correlates haploytpes with HIV progression in different racial populations (see Table 7, Table 9, Table 11; figure 3, col. 28). With regard to claim 56, Kaslow specifically teaches that 2 HHE copies increased risk of disease progression in Caucasians (col. 37).

It is noted that the claims are directed to methods whose only positive step is "using" a set of nucleic acid segments whose structural makeup is not set forth. In reciting the step of "identifying the CCR5 haploytpe group", the claim does not make clear any positive active steps for identifying. Accordingly, the claim's reliance on an unspecified set of nucleic acids does not make clear what is being assessed to determine the "CCR5 haploytpe group" of a subject, or which of the variations listed in claim 38 are determined. Accordingly, the claims have been given their broadest reasonable interpretation to encompass methods of determining alleles in the CCR5 and CCR2 genes as set forth by Kaslow.

12. Claims 49-51 and 54-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Choi (Choi et al; WO 01/77215).

Choi teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles (see page 33) using a set of nucleic acids (page 31) in different populations (table 1, page 8; page 18). Choi teaches to correlate the haplotypes with susceptibility to disease or severity of disease including HIV infection in a population and comparing with a reference population (para bridging pages 5-6).

It is noted that the claims are directed to methods whose only positive step is "using" a set of nucleic acid segments whose structural makeup is not set forth. In reciting the step of "identifying the CCR5 haploytpe group", the claim does not make clear any positive active steps for identifying. Accordingly, the claim's reliance on an unspecified set of nucleic acids does not make clear what is being assessed to determine the "CCR5 haploytpe group" of a subject, or which of the variations listed in claim 38 are determined. Accordingly, the claims have been given their broadest reasonable interpretation to encompass methods of determining alleles in the CCR5 and CCR2 genes as set forth by Choi.

13. Claims 49-51, and 53-57 are rejected under 35 U.S.C. 102(a) as being anticipated by (Gonzalez et al; PNAS, vol. 96, pages 12004-12009; October 12, 1999).

Gonzalez teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles, including detecting the CCR2 V/I mutation (claim 53) and the 32 base pair deletion in the CCR5 ORF (see Figure 1) using a set of nucleic acids. With regard to claims 50, 51, and 54-57 Gonzalez correlates haplotypes with HIV progression in different racial populations (see Fig. 5; page 788, col 1-2; page 789; figure 3) and teaches accelerated progression of disease in Caucasians with HHE/HHE, and HHC/HHC & HHC/HHD in African Americans (page 12007, col 2- page 12008, col. 1).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 49-50, 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buseyne (Buseyne et al; Journal of Infectious Diseases, October 1998, vol. 178, pages 1019-1023) in view of Mummidi.

Buseyne teaches determining the CCR5 32 base pair deletion in perinatally HIV infected children and correlating the impact of heterozygosity for the receptor with plasma viral load and CD4 T lymphocytes (see abstract). Buseyne teaches using a set of oligonucleotides for determining the presence of the mutation (see page 1020, col. 1).

Buseyne does not teach using a set of oligonucleotides capable of detecting the haplotype group in claim 38, however Mummidi teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles, including detecting the CCR2 V/I mutation (claim 53) and the 32 base pair deletion in the CCR5 ORF (see Figure 1) using a set of nucleic acids (page 792, col. 2 "Genotype analysis" to page 793 para 1 first column). Mummidi teaches correlating haploytpes with HIV progression in different populations (see page 788, col 1-2; page 789; figure 3;). Mummidi

teaches sequencing the CCR5 region from –731 - +981 (para bridging pages 792-793). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Buseyne to include determining alleles in the CCR5 promoter as taught by Mummidi for the purpose of providing a more comprehensive analysis of CCR5 and CCR2 alleles in determining disease progression in children infected with HIV. The ordinary artisan would have been motivated to improve the method of Buseyne as taught by Mummidi for the purpose of providing more comprehensive analysis of CCR5 and CCR2 alleles because Mummidi teaches that the genetic determinates of HIV are complex and teaches the use of additionally determining alleles in the CCR5 promoter for determining HIV disease progression and transmission in different populations.

17. Claims 59 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mummidi, or Kaslow, or Choi, or Gonzalez, each in view of Hogg (Hogg et al; The Lancet, vol. 349, page 1294, 1997).

Mummidi teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles, including detecting the CCR2 V/I mutation and the 32 base pair deletion in the CCR5 ORF (see Figure 1) using a set of nucleic acids (page 792, col. 2 "Genotype analysis" to page 793 para 1 first column). Mummidi teaches correlating haploytpes with HIV progression in different racial populations (see page 788, col 1-2; page 789; figure 3;). Mummidi teaches sequencing the CCR5 region from –731-+981 (para bridging pages 792-793).

Kaslow teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles, including detecting the CCR2 V/I mutation and the 32 base pair deletion in the CCR5 ORF (see

Figure 2, Figure 9) using a set of nucleic acids. Kaslow correlates haploytpes with HIV progression in different racial populations (see Table 7, Table 9, Table 11; figure 3, col. 28).

Gonzalez teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles, including detecting the CCR2 V/I mutation the 32 base pair deletion in the CCR5 ORF (see Figure 1) using a set of nucleic acids. Gonzalez correlates haplotypes with HIV progression in different racial populations (see Fig. 5; page 788, col 1-2; page 789; figure 3) and teaches accelerated progression of disease in Caucasians with HHE/HHE, and HHC/HHC & HHC/HHD in African Americans (page 12007, col 2- page 12008, col. 1).

Choi teaches detecting the CCR5 haploytpe of individuals on both CCR5 alleles (see page 33) using a set of nucleic acids (page 31) in different populations (table 1, page 8; page 18). Choi teaches to correlate the haplotypes with susceptibility to disease or severity of disease including HIV infection in a population and comparing with a reference population (para bridging pages 5-6).

Mummidi, Kaslow, Choi, and Gonzalez do not teach treating a subject identified as having increased risk of HIV-1 infection or disease progression, however Hogg teaches that a substantial decrease in AIDS related mortality was found in British Columbia which coincided with the availability of lamivudine and the expanded use of double combination retroviral therapy (last para). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to treat subjects identified at increased risk of HIV-1 infection or disease progression as taught by Mummidi or Kaslow or Choi or Gonzalez with antiretroviral therapy as taught by Hogg. The ordinary artisan would have been motivated to treat subjects identified at increased risk of HIV-1 infection or disease progression with

antiretroviral therapy because Hogg teaches that a substantial decrease in AIDS related mortality was found in British Columbia which coincided with the availability of lamivudine and the expanded use of double combination retroviral therapy.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton
Primary Examiner
Art Unit 1634
4/28/06